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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/456,306	12/08/1999	NICOLE DUSCH	PM-265182	6287
909	7590	11/03/2004	EXAMINER	
PILLSBURY WINTHROP, LLP			STEADMAN, DAVID J	
P.O. BOX 10500			ART UNIT	PAPER NUMBER
MCLEAN, VA 22102			1652	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/456,306	DUSCH ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	David J Steadman	1652	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 September 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 35-41 and 43-52 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 35-38, 40, 41 and 43-52 is/are rejected.
- 7) ☒ Claim(s) 39 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Appendices A-D</u> .                   |

**DETAILED ACTION**

***Status of the Application***

- [1]** Claims 35-41 and 43-52 are pending in the application.
- [2]** Applicants' amendment to the claims, filed September 16, 2004, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.
- [3]** Applicants' amendment to the specification, filed September 16, 2004, is acknowledged.
- [4]** Receipt of an amended abstract to the specification, filed September 16, 2004, is acknowledged.
- [5]** Receipt of a computer readable form of the sequence listing, a paper copy thereof, a statement of their sameness, and a statement that the paper copy of the sequence listing contains no new matter, all filed September 16, 2004, is acknowledged.
- [6]** Applicants' arguments filed on September 16, 2004 have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [7]** The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.
- [8]** The indicated allowability of claims 35 and 37-41 is withdrawn in view of the new rejections as set forth below.

***Claim Objections***

[9] Claim 37 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 35 encompasses any nucleic acid that encodes SEQ ID NO:2, including all degenerate variants thereof. As such, claim 37 does not further limit claim 35.

***Claim Rejections - 35 USC § 112, Second Paragraph***

[10] Claim(s) 45-46 and 50-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 45 (claim 46 dependent therefrom) and 50 (claims 51-52 dependent therefrom) are confusing in that the claims recite "the nucleic acid molecule of claim 42," however, claim 42 has been canceled. It is suggested that applicants clarify the meaning of the claims. In the interest of advancing prosecution, the examiner has interpreted claims 45 and 50 as being dependent upon claim 44 instead of claim 42.

***Claim Rejections - 35 USC § 112, First Paragraph***

[11] Claims 36, 38, 40-41, and 50-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding SEQ ID NO:2, including SEQ ID NO:1, does not reasonably provide enablement for the

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broad scope of claimed nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of polynucleotides of claims 36 (claims 38 and 40-41 dependent therefrom) and 50 (claims 51-52 dependent therefrom) for the reasons of record as set forth at item [9] of the Office action mailed June 16, 2004.

RESPONSE TO ARGUMENTS: Applicants argue the variants encompassed by the claims must retain the utility of the DNA sequence allegedly discovered by applicants. Applicants the specification enables a skilled artisan to make and use all variants encompassed within the scope of the claims using routine recombinant DNA techniques that are acknowledged by Example 14 of the Office's Revised Interim Written Description Guidelines Training Materials and pyruvate oxidase activity assays that were known in the art at the time of the invention. Applicants further argue the specification provides guidance as to the types of changes that are more likely to retain functionality. Applicants provide Attachments A and B as evidence. Applicants' argument is not found persuasive.

There is no dispute that recombinant DNA techniques for isolating and altering an encoding polynucleotide sequence and methods of assaying pyruvate oxidase enzymatic activity were known in the art at the time of the invention. It should be noted that, while the Office's Revised Interim Written Description Guidelines Training Materials

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indicate that such techniques were known in the art, applicants are reminded that "the written description requirement is separate and distinct from the enablement requirement" (MPEP 2161). The fact that such techniques were known does not necessarily indicate an enabling disclosure for the scope of claimed polynucleotide variants. In this case, the specification is silent with regard to guidance for determining which of those nucleotides of SEQ ID NO:1 can be altered with an expectation of obtaining an encoded polypeptide having pyruvate oxidase activity. While it is acknowledged that the specification provides a general discussion of mutations (p. 10, lines 15-30), this disclosure fails to provide any specific guidance regarding altering the sequence of SEQ ID NO:1. The variants encompassed by claims 36 and 50 is vast, including any variant having an insertion, addition, deletion, or substitution and any combination thereof within the identity or hybridization limitation as recited in the claims. As the claims encompass any variant as described above and in view of the lack of guidance in the specification and prior art, at the time of the invention it was highly unpredictable as to which nucleotides of SEQ ID NO:1 could have been altered while encoding a polypeptide that maintains pyruvate oxidase activity as evidenced by state of the art as represented by Branden and Witkowski et al. (cited in a previous Office action), the teachings of which are undisputed by applicants. Because the claims encompass a vast number of variants, the specification provides no specific guidance regarding alteration of SEQ ID NO:1 with an expectation of obtaining the desired variant, there is a high level of unpredictability, and the experimentation required to

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make all variants as broadly encompassed by the claims was not routine, undue experimentation is required to make all variants as encompassed by the claims.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35

U.S.C. 102 that form the basis for the rejections under this section made in this

Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

**[12]** Claim(s) 35-38, 40-41, and 43-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Pompejus et al. (US Patent Application Publication 2004/0180408 A1).

The date relied upon for applying Pompejus et al. as prior art is August 31, 1999. The claims (in relevant part) are drawn to nucleic acids encoding SEQ ID NO:2, variants thereof, vectors and host cells, and a fragment of SEQ ID NO:1.

Pompejus et al. teaches a nucleic acid, SEQ ID NO:85, encoding a polypeptide that is 100% identical to SEQ ID NO:2 of the instant application (see Appendix A) and teach fragments and complements of their nucleic acid (p. 11). Pompejus et al. teach a vector comprising their nucleic acid and a host cell comprising said vector (pp. 14-17). This anticipates claims 35-38, 40-41, and 43-52 as written.

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**[13]** It should be noted that the polynucleotide of SEQ ID NO:1 of the instant application appears to be novel over Pompejus et al. While nucleotides 227 to 2086 of SEQ ID NO:1 are identical to the full length of SEQ ID NO:85 of Pompejus et al., nucleotides 1-226 of SEQ ID NO:1 are not disclosed by Pompejus et al. Thus, Pompejus et al. does not disclose the full length of SEQ ID NO:1 of the instant application. See Appendix B.

**[14]** It should also be noted that claim 39 has not been rejected as being anticipated or made obvious by Pompejus et al. According to the specification (see p. 18, middle), vector pCR2.1poxBint has a fragment of nucleotides 705 to 1579 of SEQ ID NO:1 (see Appendix C), encoding amino acids 127 to 417 of SEQ ID NO:2 (see Appendix D). The examiner can find no teaching in the prior art of record for a pCR2.1 vector having an insert of nucleotides 705 to 1579 of SEQ ID NO:1.

### ***Conclusion***

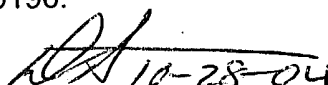
**[15]** Status of the claims:

- Claims 35-41 and 43-52 are pending.
- Claims 35-38, 40-41, and 43-52 are rejected.
- Claim 39 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:30 am to 4:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

  
David J. Steadman, Ph.D.  
Primary Examiner  
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**APPENDIX A**

RESULT 1

us-10-781-014-85

## Alignment Scores:

Pred. No.:	0	Length:	1860
Score:	2985.00	Matches:	579
Percent Similarity:	100.00%	Conservative:	0
Best Local Similarity:	100.00%	Mismatches:	0
Query Match:	100.00%	Indels:	0
DB:	1	Gaps:	0

US-09-456-306-2 (1-579) x us-10-781-014-85 (1-1860)

```
Qy      1 MetAlaHisSerTyrAlaGluGlnLeuIleAspThrLeuGluAlaGlnGlyValLysArg 20
      |||
Db    101 ATGGCACACAGCTACGCAGAACAAATTAATTGACACTTTGGAAGCTCAAGGTGTGAAGCGA 160

Qy      21 IleTyrGlyLeuValGlyAspSerLeuAsnProIleValAspAlaValArgGlnSerAsp 40
      |||
Db    161 ATTTATGGTTTGGTGGGTGACAGCCTTAATCCGATCGTGGATGCTGTCCGCCAATCAGAT 220

Qy      41 IleGluTrpValHisValArgAsnGluGluAlaAlaAlaPheAlaAlaGlyAlaGluSer 60
      |||
Db    221 ATTGAGTGGGTGCACGTTCGAAATGAGGAAGCGGCGCGTTTGACGCCGTGCGGAATCG 280

Qy      61 LeuIleThrGlyGluLeuAlaValCysAlaAlaSerCysGlyProGlyAsnThrHisLeu 80
      |||
Db    281 TTGATCACTGGGAGCTGGCAGTATGTGCTGCTTCTGTGGTCTTGAAACACACACCTG 340

Qy      81 IleGlnGlyLeuTyrAspSerHisArgAsnGlyAlaLysValLeuAlaIleAlaSerHis 100
      |||
Db    341 ATTCAGGTCTTTATGATTTCGCATCGAAATGGTGCGAAGGTGTTGGCCATCGCTAGCCAT 400

Qy     101 IleProSerAlaGlnIleGlySerThrPhePheGlnGluThrHisProGluIleLeuPhe 120
      |||
Db    401 ATTCCGAGTGCCAGATTGGTTCGACGTTCTTCCAGGAAACGCATCCGGAGATTTGTTT 460

Qy     121 LysGluCysSerGlyTyrCysGluMetValAsnGlyGlyGluGlnGlyGluArgIleLeu 140
      |||
Db    461 AAGGAATGCTCTGTTACTGCGAGATGGTGAATGGTGGTGAGCAGGGTGAACGCATTTTG 520

Qy     141 HisHisAlaIleGlnSerThrMetAlaGlyLysGlyValSerValValIleProGly 160
      |||
Db    521 CATCACGCGATTTCAGTCCACCATGGCGGGTAAAGGTGTGTCGGTGGTAGTGATTCTCGGT 580

Qy     161 AspIleAlaLysGluAspAlaGlyAspGlyThrTyrSerAsnSerThrIleSerSerGly 180
      |||
Db    581 GATATCGCTAAGGAAGACGCAGGTGACGGTACTTATTCCAATTCCACTATTCTTCTGGC 640

Qy     181 ThrProValValPheProAspProThrGluAlaAlaAlaLeuValGluAlaIleAsnAsn 200
      |||
Db    641 ACTCCTGTGGTGTTCGCGATCCTACTGAGGCTGCAGCGCTGGTGGAGGCGATTAAACAAC 700

Qy     201 AlaLysSerValThrLeuPheCysGlyAlaGlyValLysAsnAlaArgAlaGlnValLeu 220
      |||
Db    701 GCTAAGTCTGTCACTTTGTTCTGCGGTGCGGGCGTGAAGAATGCTCGCGCGAGGTGTTG 760

Qy     221 GluLeuAlaGluLysIleLysSerProIleGlyHisAlaLeuGlyGlyLysGlnTyrIle 240
      |||
Db    761 GAGTTGGCGGAGAAGATTAAATCACCGATCGGCATGCGCTGGGTGTAAGCAGTACATC 820

Qy     241 GlnHisGluAsnProPheGluValGlyMetSerGlyLeuLeuGlyTyrGlyAlaCysVal 260
      |||
Db    821 CAGCATGAGAATCCGTTTGAGGTGCGCATGTCTGGCCTGCTTGGTTACGGCGCCTGCGTG 880

Qy     261 AspAlaSerAsnGluAlaAspLeuLeuIleLeuLeuGlyThrAspPheProTyrSerAsp 280
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      |||
Db      881  GATGCGTCCAATGAGGCGGATCTGCTGATTCTATTGGGTACGGATTTCCCTTATTCTGAT 940
Qy      281  PheLeuProLysAspAsnValAlaGlnValAspIleAsnGlyAlaHisIleGlyArgArg 300
      |||
Db      941  TTCCTTCTAAAGACAACGTTGCCAGGTGGATATCAACGGTGCGCACATTGGTCGACGT 1000
Qy      301  ThrThrValLysTyrProValThrGlyAspValAlaAlaThrIleGluAsnIleLeuPro 320
      |||
Db      1001 ACCACGGTGAAGTATCCGGTGACCGGTGATGTTGCTGCAACAATCGAAAATATTTTGCCT 1060
Qy      321  HisValLysGluLysThrAspArgSerPheLeuAspArgMetLeuLysAlaHisGluArg 340
      |||
Db      1061 CATGTGAAGGAAAAACAGATCGTTCCTTCCTTGATCGGATGCTCAAGGCACACGAGCGT 1120
Qy      341  LysLeuSerSerValValGluThrTyrThrHisAsnValGluLysHisValProIleHis 360
      |||
Db      1121 AAGTTGAGCTCGGTGGTAGAGACGTACACACATAACGTCGAGAAGCATGTGCCTATTAC 1180
Qy      361  ProGluTyrValAlaSerIleLeuAsnGluLeuAlaAspLysAspAlaValPheThrVal 380
      |||
Db      1181 CCTGAATACGTTGCCTCTATTTTGAACGAGCTGGCGGATAAGGATGCGGTGTTTACTGTG 1240
Qy      381  AspThrGlyMetCysAsnValTrpHisAlaArgTyrIleGluAsnProGluGlyThrArg 400
      |||
Db      1241 GATACCGGCATGTGCAATGTGTGGCATGCGAGGTACATCGAGAATCCGGAGGGAACGCGC 1300
Qy      401  AspPheValGlySerPheArgHisGlyThrMetAlaAsnAlaLeuProHisAlaIleGly 420
      |||
Db      1301 GACTTTGTGGGTTCATTCCGCCACGGCACGATGGCTAATGCGTTGCCTCATGCCATTGGT 1360
Qy      421  AlaGlnSerValAspArgAsnArgGlnValIleAlaMetCysGlyAspGlyGlyLeuGly 440
      |||
Db      1361 GCGCAAAGTGTGATCGAAACCGCCAGGTGATCGCGATGTGTGGCGATGGTGGTTTGGGC 1420
Qy      441  MetLeuLeuGlyGluLeuLeuThrValLysLeuHisGlnLeuProLeuLysAlaValVal 460
      |||
Db      1421 ATGCTGTGTTGGGTGAGCTTCTGACCGTTAAGCTGCACCAACTTCCGCTGAAGGCTGTGGTG 1480
Qy      461  PheAsnAsnSerSerLeuGlyMetValLysLeuGluMetLeuValGluGlyGlnProGlu 480
      |||
Db      1481 TTTAACACAGTTCTTTGGGCATGGTGAAGTTGGAGATGCTCGTGGAGGACAGCCAGAA 1540
Qy      481  PheGlyThrAspHisGluGluValAsnPheAlaGluIleAlaAlaAlaGlyIleLys 500
      |||
Db      1541 TTTGGTACTGACCATGAGGAAGTGAATTTTCGAGAGATTGCGGCGGCTGCGGGTATCAAA 1600
Qy      501  SerValArgIleThrAspProLysLysValArgGluGlnLeuAlaGluAlaLeuAlaTyr 520
      |||
Db      1601 TCGGTACGCATACCGATCCGAAGAAAGTTCCGAGCAGCTAGCTGAGGCATTGGCATAT 1660
Qy      521  ProGlyProValLeuIleAspIleValThrAspProAsnAlaLeuSerIleProProThr 540
      |||
Db      1661 CCTGGACCTGTACTGATCGATATCGTCACGGATCCTAATGCGCTGTCGATCCCACCAACC 1720
Qy      541  IleThrTrpGluGlnValMetGlyPheSerLysAlaAlaThrArgThrValPheGlyGly 560
      |||
Db      1721 ATCACGTGGGAACAGGTCATGGGATTCAGCAAGGCGGCCACCCGAACCGTCTTTGGTGGA 1780
Qy      561  GlyValGlyAlaMetIleAspLeuAlaArgSerAsnIleArgAsnIleProThrPro 579
      |||
Db      1781 GGAGTAGGAGCGATGATCGATCTGGCCCGTTGCAACATAAGGAATATTCCTACTCCA 1837
```

## APPENDIX B

## RESULT 1

us-10-781-014-85

Query Match 86.1%; Score 1860; DB 1; Length 1860;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 1860; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	227	CTGGCAGGCGGGCGAAGCGTGGCAACAACCTGGAATTTAAGAGCACAAATTGAAGTCGCACC	286
Db	1	CTGGCAGGCGGGCGAAGCGTGGCAACAACCTGGAATTTAAGAGCACAAATTGAAGTCGCACC	60
Qy	287	AAGTTAGGCAACACAATAGCCATAACGTTGAGGAGTTCAGATGGCACACAGCTACGCAGA	346
Db	61	AAGTTAGGCAACACAATAGCCATAACGTTGAGGAGTTCAGATGGCACACAGCTACGCAGA	120
Qy	347	ACAATTAATTGACACTTTGGAAGCTCAAGGTGTGAAGCGAATTTATGGTTTGGTGGGTGA	406
Db	121	ACAATTAATTGACACTTTGGAAGCTCAAGGTGTGAAGCGAATTTATGGTTTGGTGGGTGA	180
Qy	407	CAGCCTTAATCCGATCGTGGATGCTGTCCGCCAATCAGATATTGAGTGGGTGCACGTTTCG	466
Db	181	CAGCCTTAATCCGATCGTGGATGCTGTCCGCCAATCAGATATTGAGTGGGTGCACGTTTCG	240
Qy	467	AAATGAGGAAGCGGCGCGTTTGCAGCCGGTGCGAATCGTTGATCACTGGGGAGCTGGC	526
Db	241	AAATGAGGAAGCGGCGCGTTTGCAGCCGGTGCGAATCGTTGATCACTGGGGAGCTGGC	300
Qy	527	AGTATGTGCTGCTTCTTGTGGTCTGGAACACACACCTGATTGAGGTCTTTATGATTC	586
Db	301	AGTATGTGCTGCTTCTTGTGGTCTGGAACACACACCTGATTGAGGTCTTTATGATTC	360
Qy	587	GCATCGAAATGGTGCGAAGGTGTTGGCCATCGCTAGCCATATTCCGAGTGCCAGATTGG	646
Db	361	GCATCGAAATGGTGCGAAGGTGTTGGCCATCGCTAGCCATATTCCGAGTGCCAGATTGG	420
Qy	647	TTCGACGTTCTTCCAGGAAACGCATCCGGAGATTTTGTTTAAGGAATGCTCTGGTTACTG	706
Db	421	TTCGACGTTCTTCCAGGAAACGCATCCGGAGATTTTGTTTAAGGAATGCTCTGGTTACTG	480
Qy	707	CGAGATGGTGAATGGTGGTGAGCAGGGTGAACGCATTTTGCATCACGCGATTCACTCCAC	766
Db	481	CGAGATGGTGAATGGTGGTGAGCAGGGTGAACGCATTTTGCATCACGCGATTCACTCCAC	540
Qy	767	CATGGCGGGTAAAGGTGTGTCGGTGGTAGTGATTCTGGTGATATCGCTAAGGAAGACGC	826
Db	541	CATGGCGGGTAAAGGTGTGTCGGTGGTAGTGATTCTGGTGATATCGCTAAGGAAGACGC	600
Qy	827	AGGTGACGGTACTTATTCCAATTCCACTATTTCTTCTGGCACTCCTGTGGTGTTCGGGA	886
Db	601	AGGTGACGGTACTTATTCCAATTCCACTATTTCTTCTGGCACTCCTGTGGTGTTCGGGA	660
Qy	887	TCCTACTGAGGCTGCAGCGCTGGTGGAGGCGATTAAACAACGCTAAGTCTGTCACTTTGTT	946
Db	661	TCCTACTGAGGCTGCAGCGCTGGTGGAGGCGATTAAACAACGCTAAGTCTGTCACTTTGTT	720
Qy	947	CTGCGGTGCGGGCGTGAAGAATGCTCGCGCGCAGGTGTTGGAGTTGGCGGAGAAGATTAA	1006
Db	721	CTGCGGTGCGGGCGTGAAGAATGCTCGCGCGCAGGTGTTGGAGTTGGCGGAGAAGATTAA	780
Qy	1007	ATCACCGATCGGGCATGCGCTGGGTGGTAAGCAGTACATCCAGCATGAGAATCCGTTTGA	1066
Db	781	ATCACCGATCGGGCATGCGCTGGGTGGTAAGCAGTACATCCAGCATGAGAATCCGTTTGA	840
Qy	1067	GGTCGGCATGTCTGGCCTGCTTGGTTACGGCGCCTGCGTGGATGCGTCCAATGAGGCGGA	1126
Db	841	GGTCGGCATGTCTGGCCTGCTTGGTTACGGCGCCTGCGTGGATGCGTCCAATGAGGCGGA	900

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Qy 1127 TCTGCTGATTCTATTGGGTACGGATTTCCTTATTCTGATTTCCTTCCTAAAGACAACGT 1186  
|||  
Db 901 TCTGCTGATTCTATTGGGTACGGATTTCCTTATTCTGATTTCCTTCCTAAAGACAACGT 960

Qy 1187 TGCCCAGGTGGATATCAACGGTGCGCACATTGGTCGACGTACCACGGTGAAGTATCCGGT 1246  
|||  
Db 961 TGCCCAGGTGGATATCAACGGTGCGCACATTGGTCGACGTACCACGGTGAAGTATCCGGT 1020

Qy 1247 GACCGGTGATGTTGCTGCAACAATCGAAAATATTTGCCTCATGTGAAGGAAAAACAGA 1306  
|||  
Db 1021 GACCGGTGATGTTGCTGCAACAATCGAAAATATTTGCCTCATGTGAAGGAAAAACAGA 1080

Qy 1307 TCGTTCCTTCTTGATCGGATGCTCAAGGCACACGAGCGTAAGTTGAGCTCGGTGGTAGA 1366  
|||  
Db 1081 TCGTTCCTTCTTGATCGGATGCTCAAGGCACACGAGCGTAAGTTGAGCTCGGTGGTAGA 1140

Qy 1367 GACGTACACACATAACGTGAGAAAGCATGTGCCTATTCACCCTGAATACGTTGCCTCTAT 1426  
|||  
Db 1141 GACGTACACACATAACGTGAGAAAGCATGTGCCTATTCACCCTGAATACGTTGCCTCTAT 1200

Qy 1427 TTTGAACGAGCTGGCGGATAAGGATGCGGTGTTACTGTGGATACCGGCATGTGCAATGT 1486  
|||  
Db 1201 TTTGAACGAGCTGGCGGATAAGGATGCGGTGTTACTGTGGATACCGGCATGTGCAATGT 1260

Qy 1487 GTGGCATGCGAGGTACATCGAGAAATCCGAGGGAACGCGCGACTTTGTGGGTTTATTCCG 1546  
|||  
Db 1261 GTGGCATGCGAGGTACATCGAGAAATCCGAGGGAACGCGCGACTTTGTGGGTTTATTCCG 1320

Qy 1547 CCACGGCACGATGGCTAATGCGTTGCCTCATGCGATTGGTGCGCAAAGTGTGATCGAAA 1606  
|||  
Db 1321 CCACGGCACGATGGCTAATGCGTTGCCTCATGCGATTGGTGCGCAAAGTGTGATCGAAA 1380

Qy 1607 CCGCCAGGTGATCGCGATGTGTGGCGATGGTGGTTTGGGCATGCTGCTGGGTGAGCTTCT 1666  
|||  
Db 1381 CCGCCAGGTGATCGCGATGTGTGGCGATGGTGGTTTGGGCATGCTGCTGGGTGAGCTTCT 1440

Qy 1667 GACCGTTAAGCTGCACCAACTTCCGCTGAAGGCTGTGGTGTTAACAACAGTTCTTTGGG 1726  
|||  
Db 1441 GACCGTTAAGCTGCACCAACTTCCGCTGAAGGCTGTGGTGTTAACAACAGTTCTTTGGG 1500

Qy 1727 CATGGTGAAGTTGGAGATGCTCGTGAGGGACAGCCAGAATTGGTACTGACCATGAGGA 1786  
|||  
Db 1501 CATGGTGAAGTTGGAGATGCTCGTGAGGGACAGCCAGAATTGGTACTGACCATGAGGA 1560

Qy 1787 AGTGAATTTGCGAGAGATTGCGGCGGCTGCGGGTATCAAATCGGTACGCATCACCGATCC 1846  
|||  
Db 1561 AGTGAATTTGCGAGAGATTGCGGCGGCTGCGGGTATCAAATCGGTACGCATCACCGATCC 1620

Qy 1847 GAAGAAAGTTGCGGAGCAGCTAGCTGAGGCATTGGCATATCCTGGACCTGTACTGATCGA 1906  
|||  
Db 1621 GAAGAAAGTTGCGGAGCAGCTAGCTGAGGCATTGGCATATCCTGGACCTGTACTGATCGA 1680

Qy 1907 TATCGTCACGGATCCTAATGCGCTGTGATCCCACCAACCATCACGTGGGAACAGGTCAT 1966  
|||  
Db 1681 TATCGTCACGGATCCTAATGCGCTGTGATCCCACCAACCATCACGTGGGAACAGGTCAT 1740

Qy 1967 GGGATTTCAGCAAGGCGGCCACCCGAACCGTCTTTGGTGGAGGAGTAGGAGCGATGATCGA 2026  
|||  
Db 1741 GGGATTTCAGCAAGGCGGCCACCCGAACCGTCTTTGGTGGAGGAGTAGGAGCGATGATCGA 1800

Qy 2027 TCTGGCCCGTTTCGAACATAAGGAATATTCTACTCCATGATGATTGATACACCTGCTGTT 2086  
|||  
Db 1801 TCTGGCCCGTTTCGAACATAAGGAATATTCTACTCCATGATGATTGATACACCTGCTGTT 1860

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**APPENDIX C**

RESULT 1

us-09-456-306-1

Query Match 100.0%; Score 875; DB 1; Length 2160;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 875; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1  TGCGAGATGGTGAATGGTGGTGAGCAGGGTGAACGCATTTTGCATCACGCGATTTCAGTCC 60
      |||
Db      705 TGCGAGATGGTGAATGGTGGTGAGCAGGGTGAACGCATTTTGCATCACGCGATTTCAGTCC 764

Qy      61  ACCATGGCGGGTAAAGGTGTGTCTGGTGGTAGTGATTCTGGTGATATCGCTAAGGAAGAC 120
      |||
Db      765  ACCATGGCGGGTAAAGGTGTGTCTGGTGGTAGTGATTCTGGTGATATCGCTAAGGAAGAC 824

Qy     121  GCAGGTGACGGTACTTATTCCAATTCCTACTTTCTTCTGGCACTCCTGTGGTGTTCCTCG 180
      |||
Db     825  GCAGGTGACGGTACTTATTCCAATTCCTACTTTCTTCTGGCACTCCTGTGGTGTTCCTCG 884

Qy     181  GATCCTACTGAGGCTGCAGCGCTGGTGGAGGCGATTAAACAACGCTAAGTCTGTCACTTTG 240
      |||
Db     885  GATCCTACTGAGGCTGCAGCGCTGGTGGAGGCGATTAAACAACGCTAAGTCTGTCACTTTG 944

Qy     241  TTCTGCGGTGCGGGCGTGAAGAATGCTCGCGCGCAGGTGTTGGAGTTGGCGGAGAAGATT 300
      |||
Db     945  TTCTGCGGTGCGGGCGTGAAGAATGCTCGCGCGCAGGTGTTGGAGTTGGCGGAGAAGATT 1004

Qy     301  AAATCACCAGTACGGGCGATGCGCTGGGTGGTAAGCAGTACATCCAGCATGAGAATCCGTTT 360
      |||
Db    1005  AAATCACCAGTACGGGCGATGCGCTGGGTGGTAAGCAGTACATCCAGCATGAGAATCCGTTT 1064

Qy     361  GAGGTGCGGCATGTCTGGCCTGCTTGGTTACGGCGCCTGCGTGGATGCGTCCAATGAGGCG 420
      |||
Db    1065  GAGGTGCGGCATGTCTGGCCTGCTTGGTTACGGCGCCTGCGTGGATGCGTCCAATGAGGCG 1124

Qy     421  GATCTGCTGATTCTATTGGGTACGATTTCCTTTATTCTGATTTCCTTCCTAAAGACAAC 480
      |||
Db    1125  GATCTGCTGATTCTATTGGGTACGATTTCCTTTATTCTGATTTCCTTCCTAAAGACAAC 1184

Qy     481  GTTGCCAGGTGGATATCAACGGTGCACACATTGGTCGACGTACCACGGTGAAGTATCCG 540
      |||
Db    1185  GTTGCCAGGTGGATATCAACGGTGCACACATTGGTCGACGTACCACGGTGAAGTATCCG 1244

Qy     541  GTGACCGGTGATGTTGCTGCAACAATCGAAAATATTTTGCCTCATGTGAAGGAAAAACA 600
      |||
Db    1245  GTGACCGGTGATGTTGCTGCAACAATCGAAAATATTTTGCCTCATGTGAAGGAAAAACA 1304

Qy     601  GATCGTTCCTTCCTTGATCGGATGCTCAAGGCACACGAGCGTAAGTTGAGCTCGGTGGTA 660
      |||
Db    1305  GATCGTTCCTTCCTTGATCGGATGCTCAAGGCACACGAGCGTAAGTTGAGCTCGGTGGTA 1364

Qy     661  GAGACGTACACACATAACGTCGAGAAGCATGTGCCTATTACCCCTGAATACGTTGCCTCT 720
      |||
Db    1365  GAGACGTACACACATAACGTCGAGAAGCATGTGCCTATTACCCCTGAATACGTTGCCTCT 1424

Qy     721  ATTTTGAACGAGCTGGCGGATAAGGATGCGGTGTTTACTGTGGATACCGGCATGTGCAAT 780
      |||
Db    1425  ATTTTGAACGAGCTGGCGGATAAGGATGCGGTGTTTACTGTGGATACCGGCATGTGCAAT 1484

Qy     781  GTGTGGCATGCGAGGTACATCGAGAATCCGGAGGGAACGCGGACTTTGTGGGTTTCATTC 840
      |||
Db    1485  GTGTGGCATGCGAGGTACATCGAGAATCCGGAGGGAACGCGGACTTTGTGGGTTTCATTC 1544

Qy     841  CGCCACGGCACGATGGCTAATGCGTTGCCTCATGC 875
      |||
Db    1545  CGCCACGGCACGATGGCTAATGCGTTGCCTCATGC 1579
```

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**APPENDIX D**

## RESULT 1

us-09-456-306-3

## Alignment Scores:

Pred. No.:	0	Length:	875
Score:	1518.00	Matches:	291
Percent Similarity:	100.00%	Conservative:	0
Best Local Similarity:	100.00%	Mismatches:	0
Query Match:	50.85%	Indels:	0
DB:	1	Gaps:	0

us-09-456-306-2 (1-579) x us-09-456-306-3 (1-875)

```
Qy      127 CysGluMetValAsnGlyGlyGluGlnGlyGluArgIleLeuHisHisAlaIleGlnSer 146
         |||
Db       1  TGCAGATGGTGAATGGTGGTGAAGGGTGAACGCATTTGCATCACGCGATTCAAGTCC 60

Qy      147 ThrMetAlaGlyLysGlyValSerValValValIleProGlyAspIleAlaLysGluAsp 166
         |||
Db       61  ACCATGGCGGGTAAAGGTGTGTGGTGGTAGTGATTCTCTGGTATATCGCTAAGGAAGAC 120

Qy      167 AlaGlyAspGlyThrTyrSerAsnSerThrIleSerSerGlyThrProValValPhePro 186
         |||
Db      121  GCAGGTGACGGTACTTATTCCAATCCACTATTTCTTCTGGCACTCCTGTGGTGTCCCG 180

Qy      187 AspProThrGluAlaAlaAlaLeuValGluAlaIleAsnAsnAlaLysSerValThrLeu 206
         |||
Db      181  GATCCTACTGAGGCTGCAGCGCTGGTGGAGGCGATTAAACAACGCTAAGTCTGTCACTTTG 240

Qy      207 PheCysGlyAlaGlyValLysAsnAlaArgAlaGlnValLeuGluLeuAlaGluLysIle 226
         |||
Db      241  TTCTGCGGTGCGGGCGTGAAGAATGCTCGCGCGCAGGTGTTGGAGTTGGCGGAGAAGATT 300

Qy      227 LysSerProIleGlyHisAlaLeuGlyGlyLysGlnTyrIleGlnHisGluAsnProPhe 246
         |||
Db      301  AAATCACCATCGGGCATGCGCTGGTGGTAAGCAGTACATCCAGCATGAGAATCCGTTT 360

Qy      247 GluValGlyMetSerGlyLeuLeuGlyTyrGlyAlaCysValAspAlaSerAsnGluAla 266
         |||
Db      361  GAGGTGCGCATGTCTGGCTGCTTGGTTACGGCGCCTGCGTGGATGCGTCCAATGAGGCG 420

Qy      267 AspLeuLeuIleLeuLeuGlyThrAspPheProTyrSerAspPheLeuProLysAspAsn 286
         |||
Db      421  GATCTGCTGATTCTATTGGGTACGGATTTCCTTATTCTGATTTCCTTCTAAAGACAAC 480

Qy      287 ValAlaGlnValAspIleAsnGlyAlaHisIleGlyArgArgThrThrValLysTyrPro 306
         |||
Db      481  GTTGCCAGGTGGATATCAACGGTGCACATTTGGTGCACGTACCACGGTGAAGTATCCG 540

Qy      307 ValThrGlyAspValAlaAlaThrIleGluAsnIleLeuProHisValLysGluLysThr 326
         |||
Db      541  GTGACCGGTGATGTTGCTGCAACAATCGAAAAATTTTGCCTCATGTGAAGGAAAAACA 600

Qy      327 AspArgSerPheLeuAspArgMetLeuLysAlaHisGluArgLysLeuSerSerValVal 346
         |||
Db      601  GATCGTTCTTCTTGTATCGGATGCTCAAGGCACACGAGCGTAAGTTGAGCTCGGTGGTA 660

Qy      347 GluThrTyrThrHisAsnValGluLysHisValProIleHisProGluTyrValAlaSer 366
         |||
Db      661  GAGACGTACACATAACGTCGAGAAGCATGTGCCTATTACCCCTGAATACGTTGCCTCT 720

Qy      367 IleLeuAsnGluLeuAlaAspLysAspAlaValPheThrValAspThrGlyMetCysAsn 386
         |||
Db      721  ATTTTGAACGAGCTGGCGGATAAGGATGCGGTGTTTACTGTGGATACCGGCATGTGCAAT 780

Qy      387 ValTrpHisAlaArgTyrIleGluAsnProGluGlyThrArgAspPheValGlySerPhe 406
```

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Db 781 GTGTGGCATGCGAGGTACATCGAGAATCCGGAGGGAACGCGGACTTTGTGGGTTTCATTC 840

Qy 407 ArgHisGlyThrMetAlaAsnAlaLeuProHis 417

Db 841 CGCCACGGCACGATGGCTAATGCGTTGCCTCAT 873